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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,200	02/06/2001	John Kisiday	01997/537001	8784
24280	7590	08/17/2004		
Choate, Hall & Stewart Exchange Place 53 State Street Boston, MA 02109			EXAMINER NAFF, DAVID M	
			ART UNIT 1651	PAPER NUMBER

DATE MAILED: 08/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/778,200

Applicant(s)

KISIDAY ET AL

Examiner

David M. Naff

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 19, 20, 22-24 and 27-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 20 is/are allowed.
- 6) ☒ Claim(s) 1-8, 19, 22-24 and 27-32 is/are rejected.
- 7) ☒ Claim(s) 20 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for
5 continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/4/04 has been entered.

10 An amendment of 6/4/04 canceled claims 9-18, 25 and 26, and amended claim 31.

Claims examined on the merits are 1-8, 19, 20, 22-24 and 27-32, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

15 ***Claim Rejections - 35 USC § 103***

Claims 1-3, 5-8, 19, 20, 22-24 and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes et al (5,955,343) in view of Hubbell (6,129,761) for the type of reasons set forth in the previous office action of 1/2/04 and for reasons herein.

20 The claims are drawn to a scaffold containing amphiphilic peptides having alternating hydrophobic and hydrophilic amino acids, which are self-assembled into a beta-sheet to encapsulate cells in the scaffold.

25 Holmes et al (col 11, lines 32-35) disclose culturing cells on a membrane or matrix formed by self-assembling of peptides as required

by the present claims. The peptides are stable in aqueous solution and self-assemble into a macroscopic structure or matrix when exposed to salt (col 1, lines 32-35). The structures produced can also encapsulate cells since the pore size of the structure is large enough
5 to allow nutrients and products to diffuse, and cells being larger than the pores are contained (col 12, lines 4-9).

Hubbell discloses a scaffold for implanting containing cells encapsulated in a hydrogel (col 5, lines 55-60), and which can contain biologically active agents such as therapeutic agents (col 7, lines
10 15-21). The hydrogel is produced by forming a polymer solution containing cells and crosslinking the polymer.

Rather than culture the cells on the membrane or matrix of Holmes et al, it would have been obvious to encapsulate the cells in the membrane or matrix as suggested by Hubbell encapsulating cells in a
15 hydrogel for implanting and by Holmes et al disclosing encapsulating cells in the membrane or matrix as an alternative to attaching cells to the membrane or matrix. The membrane or matrix of Holmes et al is inherently a scaffold. The peptides of Holmes et al may be combined with collagen (col 11, lines 26-28), which is an extracellular matrix
20 protein. Chondrocytes disclosed by Hubbell et al (col 11, line 58) produce extracellular matrix protein, and it would have been obvious to use chondrocytes to produce the collagen disclosed by Holmes et al. The collagen would have inherently resulted in an increase in strength, stiffness and equilibrium compression modulus as required by
25 certain dependent claims. Growth factors as disclosed by Holmes et al

Art Unit: 1651

(col 11, lines 35-38) would be a chemoattractant as in claim 2. Additionally, the membrane or matrix of Holmes et al may contain a therapeutic agent (col 11, lines 3-11) as in claim 2. The condition of claim 8 would be inherent when encapsulating cells in the membrane or matrix of Holmes et al. Compression that can be within the scope of claim 30 would not result in a different membrane or matrix than obtained by Holmes et al. Handling the membrane or matrix of Holmes et al will inherently result in applying some compression. Hubbell et al disclose molding (col 12, line 22) and would have suggested pre-shaping as in claim 29. Selecting an optimum amount of cells as in claim 31 for a particular function would have been within the skill of the art. Cells encapsulated in the membrane or matrix of Holmes et al will inherently divide as in claim 32 after being placed in a culture medium as suggested by Holmes et al (col 12, lines 1-9). Peptides used by Holmes et al inherently have an adhesion site as in claim 3.

Response to Arguments

Applicants urge that Hubbell does not suggest encapsulating cells in the membrane of Holmes et al. However, Hubbell is not applied alone for suggesting encapsulating cells in the membrane, but is combined with Holmes et al disclosing that cells can be encapsulated in the membrane (col 12, lines 5-9). Holmes et al forming the membrane fast and Hubbell slowly polymerizing does not make unobvious that cells can be encapsulated in the membrane. Self-assembly of the peptides of Holmes et al does not occur until after a salt is added. Obviously, cells can be combined with the peptides before the salt is

added so that self-assembly will occur in the presence of the cells and result in entrapment of the cells in the membrane or matrix. While Holmes et al may not explicitly describe how cells can be encapsulated, it is believed how to encapsulate the cells would be obvious to one of ordinary skill in the art when Hubbell is also considered, and suggesting that cells can be encapsulated simply by adding cells to the peptides before self-assembly and allow self-assembly to occur in the presence of the peptides. This would be apparent from Hubbell crosslinking a polymer in presence of cells to encapsulate the cells in a crosslinked polymer. Incubating cells and peptides under conditions that do not allow self-assembly, and then add an electrolyte to cause the peptides to self-assemble would have been obvious from Holmes et al disclosing that the peptides do not self-assemble in aqueous solution until a salt is added. This procedure would have been an obvious method to use when encapsulating cells as suggested by Holmes et al (col 12, lines 5-10), and is also suggested by Hubbell mixing cells with a polymer solution and then crosslinking the polymer to form a hydrogel. Apparently Holmes et al believed that encapsulated cells in the self-assembled peptide matrix can survive, or otherwise encapsulating cells would not have been mentioned. There is nothing to suggest that self-assembly of peptides while cells are present will cause cells not to survive. Cells surviving crosslinking of a polymer to form a hydrogel as disclosed by Hubbell would have led one to expect that cells can also survive self-assembly of peptides. The structure of a matrix formed by self-

assembly of peptides is not sufficiently different from a matrix formed by crosslinking a polymer to lead one to believe that cells cannot survive in the self-assembled peptide matrix.

Applicants urge that Hubbell was published in 1996 as shown by
5 exhibit B three years after the Holmes et al invention of self-assembly of peptides, and Hubbell does not mention self-assembly of peptides to encapsulate cells. However, this does not make the claimed invention unobvious since Hubbell may not have known about the Holmes et al invention when the Hubbell application for patent was
10 filed. This also applies to exhibit A showing Holmes et al disclosing self-assembly of peptides before the invention of Hubbell. Holmes et al clearly considered self-assembly of peptides to encapsulate cells to be useful way to encapsulate cells, and it would have been obvious to follow the teachings of Holmes et al without
15 Hubbell disclosing the use of self-assembly of peptides to encapsulate cells.

In regard to exhibit C, the present invention being published in a scientific journal does not establish that the invention is unobvious. There is no evidence establishing that publication depends
20 on the work done being unobvious. The disclosure of exhibit D in regard to the present invention was published after the present application was filed, and cannot render the invention unobvious at the time present application was filed. Furthermore, Hubbell mentioning the invention in exhibit D does not mean that Hubbell
25 considered the invention unobvious. Hubbell makes no statement in

regard to being obvious or unobvious. Moreover, such a statement would be a matter of opinion. The exhibit does not state that self-assembled peptides are ECM-like, but rather states that ECM-like material is desirable. In the last paragraph on page 555 of exhibit
5 D, after mentioning reference 91, it is stated that technical hurdles are still to be overcome. This indicates that Hubbell did not consider the present invention to be a final solution to the problem of obtaining an acceptable ECM-like material.

In regard to claim 19, while Holmes et al may envision combining
10 peptides and collagen as asserted by applicants, it would have been obvious when Hubbell is considered that chondrocytes (col 7, line 8) can be the encapsulated cells of Holmes et al, and the function of these cells to produce extracellular matrix protein is well known.

As to arguments concerning claim 30, this claim contains no
15 limitation as to the amount and form of compression applied other than being static or dynamic, and the claim does not exclude incidental compression resulting from normal handling. The specification cannot put a limitation in the claim that is not in the claim. Claim limitations can be given their broadest reasonable interpretation.
20 The claim encompasses very small amounts of compression that will not change the scaffold from that without compression, and will not provide the equilibrium compression modulus disclosed in the specification.

Art Unit: 1651

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-3, 5-8, 19, 20, 22-24 and 27-32 above, and further in view of Holmes et al (PNAS).

The claim requires cells encapsulated to be neurons.

5 Holmes et al (PNAS) disclose attaching neurons to a self-assembling peptide scaffold and growing the neurons.

When encapsulating cells in a self-assembling peptide membrane or matrix as set forth above, it would have been obvious to use neurons as the cells to obtain the function of neurons as suggested by Holmes et al (PNAS) attaching neurons to a self-assembling peptide scaffold.
10 Holmes et al (PNAS) further disclose that the peptides self-assemble to form a hydrogel (first page, left col, about line 8).

Response to Arguments

Applicants rely on arguments traversing the above rejection to
15 traverse this rejection. These arguments are unpersuasive for reasons set forth above.

Conclusion

Claim 20 is allowable, but is objected to as being dependent on a rejected claim.

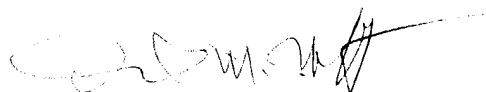
20 Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful,
25 the examiner's supervisor, Mike Wityshyn can be reached on 571-272-

Art Unit: 1651

0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David M. Naff
Primary Examiner
Art Unit 1651

DMN

15 8/13/04